**UNITED STATES DISTRICT COURT**
**FOR THE WESTERN DISTRICT OF WISCONSIN**

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| PROMEGA CORPORATION, ET AL.<br><br>Plaintiff,<br><br>vs.<br><br>LIFE TECHNOLOGIES CORPORATION, INVITROGEN IP HOLDINGS, INC., AND APPLIED BIOSYSTEMS, LLC,<br><br>Defendants. | Civil Action No. 10-CV-281 |

**DEFENDANTS' RESPONSE TO PROMEGA CORPORATION'S OPENING CLAIM CONSTRUCTION BRIEF**

Defendants Life Technologies Corporation ("Life Technologies"), Invitrogen IP Holdings, Inc. ("Invitrogen"), and Applied Biosystems, LLC ("Applied Biosystems") (collectively, "Defendants") submit their Response to Promega Corporation's ("Promega") Opening Claim Construction Brief (Dkt. # 154) ("Promega Br.").

## I. INTRODUCTION

While Defendants' proposed constructions are supported on all sides by the totality of the intrinsic record, Promega seeks instead to bypass this highly relevant guide to the meaning of claims. Incredibly, nowhere in its brief does it even mention the extensive prosecution histories of the Promega patents.[1] Instead, Promega takes an alternate route to arrive at its proposed constructions, one involving shortcuts in the form of alleged procedural bars (issue preclusion), hypothetical technicalities, claim differentiation, and selected and edited sound bites taken out of

[1] U.S. Patent Nos. 5,843,660; 6,221,598; 6,479,235; and 7,008,771.

context. Many of Promega's proposed constructions are contradicted by its own statements in the intrinsic record and/or fail to make sense from a technical standpoint.

Promega's proposed constructions and supporting arguments are also entirely disconnected from the alleged inventions themselves and the state of the art. The intrinsic record in this case paints a rich and detailed picture of the state of the art, without which it is impossible to understand what Promega was seeking to achieve and in the end what if anything Promega actually invented. It is no wonder, therefore, that Promega's proposed constructions, disconnected from the proper temporal and technological context, do not accurately reflect the scope of what it allegedly invented. Unsurprisingly, they are much broader. In reality, the intrinsic evidence overwhelmingly demonstrates that what Promega allegedly invented was limited to methods and materials for multiplexing specific and closed sets of short tandem repeat (STR) loci using specific primer sequences. The possibility that Promega invented ways to multiplex open-ended sets of loci using different or additional loci or primers from those listed in the claims and specifications is absolutely foreclosed by Promega's well-documented admissions in the intrinsic evidence. As Promega itself argued, multiplex reactions were notoriously laborious endeavors involving extensive trial and error, and skilled artisans could not predict with any reasonable degree of certainty what effect adding even a single locus to a given set would have on the viability of a multiplex reaction.

In the end, Defendants' proposed constructions should prevail. These constructions are informed by the rich context of the intrinsic evidence and the claims as a whole, and therefore impart a claim scope truly commensurate with the scope of the alleged inventions.

## II. ARGUMENT

The claim terms identified by Defendants for construction appear as limitations in one or more of the asserted claims of the Promega patents, contrary to Promega's suggestion otherwise. Promega Br. at 14, Ex. B. Appended hereto as Appendix A is a chart showing where the claim terms identified by Defendants appear in the asserted claims, correcting errors in Exhibit B of Promega's brief.

### A. DEFENDANTS' PROPOSED CONSTRUCTIONS ARE GROUNDED IN THE INTRINSIC RECORD WHILE PROMEGA SEEKS TO CIRCUMVENT IT

#### i. "a set of . . . loci"

| Defendants' Proposed Construction | Promega's Proposed Construction |
|---|---|
| a collection of only the loci listed in the claim | none of the asserted claims that require a multiplex of a defined set of loci exclude the presence of other STR loci in that required multiplex reaction[2] |

##### a. The Specifications and Prosecution Histories Show that the Alleged Inventions Were Closed Sets of Specific Loci

Claim construction requires the Court to ascertain what an inventor actually invented. Smith v. Snow, 294 U.S. 1, 14 (1935) (the claims should be construed to "secure to the patentee his ***actual invention***") (emphasis added); Phillips v. AWH Corp., 415 F.3d 1303, 1321 (Fed. Cir. 2005) ("The patent system is based on the proposition that the claims cover ***only the invented subject matter***.") (emphasis added); Acumed, LLC v. Stryker Corp., 483 F.3d 800, 815 (Fed. Cir. 2007) (advising that "[p]atent scope should be coextensive with what the inventor invented"). As discussed extensively in Defendants' opening brief, the specifications and prosecution histories of the Promega patents reveal that the alleged inventions of the Promega patents are in

[2] While Promega argues that an earlier claim construction of the Court is binding in the present action and purports to base its proposed constructions on the earlier construction, it in fact rewrites it. *See* Sun Decl., Ex. 17. In any case, as discussed below, *infra* Part II.B, the earlier claim construction is not binding in the present case.

fact very narrow in scope, and in particular were limited to ***closed*** sets of ***specific*** loci. *See* Defendants' Memorandum in Support of Motion Requesting Claim Construction ("Defendants Br.") (Dkt. #158) at 10-17. They were conceived against a state of the art that was rife with failure, unpredictability, and extensive trial and error experimentation. *See generally* id., Appendix A. According to Promega, in designing a successful multiplex reaction, skilled artisans were required to optimize a "multitude of parameters" through "arduous" trial and error and which in many cases "still [led] only to failure." Id. at 12 (citation omitted). Moreover, they "[could] not predict with any reasonable degree of certainty" whether a given set of loci would co-amplify "until the co-amplification action was attempted and successfully performed." Id. at 11-12 (citations omitted). Even after a successful multiplex reaction was achieved, adding new or additional loci to the multiplex essentially required redesigning a new reaction from scratch, as different loci interact with each other in different and unpredictable ways. Id. at 33.

The intrinsic record shows that Promega did not overcome these difficulties in a broad, far-reaching manner which enabled skilled artisans to thereafter multiplex open-ended sets of loci, unbounded to an upper limit. Rather, at most what Promega discovered was ways to multiplex specific, closed sets of loci—those sets of loci described in the examples in the specifications and listed in the claims. Indeed, during prosecution Promega repeatedly took the position that its alleged inventions overcame the prior art because they disclosed specific sets of loci different from the sets of loci disclosed in the prior art. Id. at 14-15. Appendix B of Defendants' brief demonstrates how insistent Promega was in this regard. Promega might have argued that it discovered more than just ways of co-amplifying specific sets of loci, thus overcoming the prior art, but it never did. Instead, over and over Promega made abundantly

clear that the specific sets of loci were the allegedly inventive aspect of the Promega patents. Id., Appendix B.

The specifications tell the same story and reinforce the only conclusion that can be drawn from the many statements made by Promega in the prosecution histories. For example, in the Summary of the Invention of each of the Promega patents, Promega states that the object of the alleged inventions was to provide methods and materials for co-amplifying "distinct [*i.e.*, specific] polymorphic short tandem repeat (STR) loci," and that "the sets of ***specific*** STR loci disclosed herein [had] not been previously described in the prior art." Id. at 8, 13-14 (emphasis added).

The unpredictability of the art and Promega's own statements in the specifications and prosecution histories foreclose any conclusion that Promega actually invented methods and materials for co-amplifying open-ended sets of loci. Capon v. Eshhar, 418 F.3d 1349, 1358 (Fed. Cir. 2005) ("It is well recognized that in the 'unpredictable' fields of science, it is appropriate to recognize the variability in the science in determining the scope of coverage to which the inventor is entitled."). At most, Promega discovered ways to multiplex certain specific sets of loci and therefore at most is entitled to claim scope limited to those loci. Smith, 294 U.S. at 14; Acumed, 483 F.3d at 815; Phillips, 415 F.3d at 1321.

**b. A Construction Based Only Upon Isolated Words in the Claims Does Not Constitute a Proper Construction**

According to Promega, words such as "at least" and "comprising" in the claims conclusively establish that the claims encompass loci not listed therein. Promega Br. at 19-20. Several of the claims recite a set of "at least" *n* loci or a set of loci "comprising" certain specific loci listed in the claims, however a cursory review of isolated words and phrases, without more, does not constitute a sufficient basis for a proper claim construction. Kyocera Wireless Corp. v.

ITC, 545 F.3d 1340, 1347 (Fed. Cir. 2008) ("[T]his court does not interpret claim terms in a vacuum, devoid of the context of the claim as a whole."); Hockerson-Halberstadt, Inc. v. Converse, Inc., 183 F.3d 1369, 1374 (Fed. Cir. 1999) ("[P]roper claim construction . . . demands interpretation of the entire claim in context, not a single element in isolation."). In particular, analysis of common claim terminology such as "at least" and "comprising" takes no account of the particular alleged inventions at issue in this case, which should be the focus of the inquiry at claim construction. Smith, 294 U.S. at 14; Acumed, 483 F.3d at 815; Phillips, 415 F.3d at 1321.

Furthermore, with respect to transition phrases such as "comprising," it is necessary to distinguish the claim elements upon which the phrase does and does not operate. The term "comprising" "does not reach into [and] render every word and phrase" within a claim open-ended. Dippin' Dots v. Mosey, 476 F.3d 1337, 1343 (Fed. Cir. 2007). *See also* Sandisk Corp. v. Kingston Tech. Co., Inc., No. 10-cv-243-bbc, 2011 U.S. Dist. LEXIS 27696, at *59 (W.D. Wis. Mar. 15, 2011). For a comprehensive discussion on the nature and effect of the term "comprising," the Court is referred to Defendants' opening brief. *See* Defendants Br. at 18-20. The end result is that the transition phrase "comprising," while presumptively rendering claims non-exclusive as to the recited claim elements, does not render the individual claim elements themselves—such as "a set of . . . loci"—open-ended.

**c. The Claim Language Requires the Same Closed Set of Specific Loci in Each and Every Step of the Method Claims**

The method claims of the Promega patents generally involve the steps of (a) obtaining a DNA sample, (b) selecting "a set of . . . loci" of interest from the DNA sample, (c) co-amplifying the set of loci, and (d) evaluating the amplified alleles from the set. Promega proposes a construction whereby the "a set of . . . loci" initially selected—even a closed set of specific

loci—can nevertheless differ from the set of loci ultimately co-amplified and evaluated. In doing so, Promega would have the Court adopt a construction irreconcilable with the claim language.

Asserted independent claim 16 of the '660 patent is an exemplary method claim and recites in relevant part (with added emphasis):

> (b) selecting a set of three short tandem repeat loci of the DNA sample to be analyzed ***which can be amplified together***, wherein the set of three loci is selected from the group of sets of loci consisting of:
>
> D3S1539, D19S253, D13S317;
> D10S1239, D9S930, D20S481;
> D10S1239, D4S2368, D20S481;
> D10S1239, D9S930, D4S2368;
> D16S539, D7S820, D13S317; and
> D10S1239, D9S930, D13S317. [sic]
>
> (c) co-amplifying the three loci in the set in a multiplex amplification reaction, wherein ***the*** product of the reaction ***is*** a mixture of amplified alleles from each of the co-amplified loci ***in the set***;

Under Promega's proposed construction, the multiplex amplification reaction of step (c) may include additional loci not selected in step (b). However, step (c) specifies "***the*** product of the reaction," meaning that there is one and only one reaction product. Further, the claim defines not what that product "comprises" or "includes" but rather what it "***is***," meaning that the definition that follows is comprehensive as well as exclusive. What "the" product of the reaction "is" is underlined above, *i.e.*, "a mixture of amplified alleles from each of the co-amplified loci ***in the set***." Because the language "in the set" finds its antecedent basis from the "set" recited in step (b), the set of loci co-amplified in step (c) must be the same as the set of loci selected in step (b).[3]

[3] The claims of the '598 patent originally recited "the product of the reaction," like the '660 and other Promega patents. However, during prosecution the examiner found this instance of the word "the" to be indefinite for lack of antecedent basis. Sun Decl., Ex. 3 at 101. Promega amended the claims to recite "thereby producing" to overcome the rejection. Id. at 153. In reality the rejection was uncalled for, as the word "the" was not an invalid reference to a

Moreover, step (b) requires that the loci selected in that step "can be amplified together," highlighting the fact that selecting any arbitrary set of loci will not satisfy the claim. As discussed in Defendants' opening brief, at the time of the alleged inventions of the Promega patents, designing a successful multiplex amplification reaction was a difficult and arduous process requiring extensive experimentation and unpredictable results. *See* Defendants Br. at 10-17. Loci which successfully amplified in a monoplex environment may have simply and inexplicably failed to amplify in a multiplex environment. *See* id. Therefore, the very purpose of "selecting" loci in step (b) is to ensure that the "co-amplifying" the loci in step (c) is not only successful, but actually possible in the first instance. This is clear from the language "which can be amplified together" in the claims. Given the unpredictability of the art in question, to open step (c) to additional loci not specifically selected in step (b) would not make sense from a technical standpoint because it would create an inoperable multiplex.

The claim language is therefore clear that the set of loci in step (b) is the exact same set of loci in step (c), without addition, subtraction, or variation. Promega itself appears to concede the fact in its brief, explaining that the Promega patents cover a method for "selecting 'a set of . . . [STR] loci'" and "'co-amplifying' the alleles of ***the selected*** loci." Promega Br. at 6 (emphasis added). Promega's proposed construction, which permits divergence between the loci in step (b) and step (c), conflicts with the claim language and therefore should not be adopted in the instant case.

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nonexistent antecedent (indeed, it would not make sense for there to be *any* product of the reaction preceding the co-amplifying step). Rather, the word "the" signifies that there is only a single, exclusive reaction product generated from the co-amplification step. As Promega intended "thereby producing" to be an equivalent of and substitution for "the product of the reaction," the above argument with respect to "the product of the reaction" applies equally to the '598 patent.

**d. The Specifications and Prosecution Histories Also Require the Same Closed Set of Specific Loci in Each and Every Step of the Method Claims**

During prosecution, Promega itself repeatedly characterized the "selecting" and "co-amplifying" steps as inextricably linked. It thus viewed the set of loci selected in step (b) and the set of loci co-amplified in step (c) as one and the same. *See* Phillips, 415 F.3d at 1318 ("[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it otherwise would be.") (citation omitted).

For example, Promega emphasized the "unpredictability of selection ***for*** co-amplification" in attempting to overcome the prior art. Sun Decl., Ex. 3 at 157 (emphasis added).[4] Promega further claimed that the prior art "failed to provide any guidance which would have suggested to one of ordinary skill in the art to ***select*** any of the sets of at least three STR loci ***co-amplified*** with the methods or using the kits of the present invention." Id. at 158 (emphasis added); Sun Decl., Ex. 4 at 251. In fact, Promega contemplated that the set of loci selected in step (b) was not only the same as the set of loci co-amplified in step (c) but also the set of loci evaluated in step (d), which recites (in claim 16 of the '660 patent):

> (d) evaluating the amplified alleles in ***the mixture*** to determine the alleles present at each of the loci analyzed in ***the set*** within ***the DNA sample***.

Sun Decl., Ex. 6 ('660 patent), col. 63, ll. 46-48 (emphasis added). The language is the same or similar for the other method claims of the '660 patent, as well as the method claims of the other Promega patents.

[4] This statement is found in the prosecution history of the '598 patent, but the "selecting" and "co-amplifying" steps are common to all of the method claims of the '660, '598, and '235 patents. (The '771 patent does not recite any method claims.)

During prosecution, Promega explained that "the ***selection*** of the specific sets of STR loci suitable for ***co-amplification*** and ***evaluation*** of the resulting mixture of amplified alleles requires taking into account a multitude of factors." Sun Decl., Ex. 4 at 251 (emphasis added). In other words, Promega viewed the method steps as interrelated and as being performed upon the same object set of loci. In addition, the emphasized claim terms in step (d) above all find their antecedent bases in steps (b) and (c) of the claims, again indicating how inextricably linked the method steps are to each other. Furthermore, none of the examples in the specifications of the Promega patent utilize different sets of loci for each successive method step. Taken together, it is clear that the claimed methods of the Promega patents do not contemplate selecting one set of loci, co-amplifying another set of loci, and evaluating yet still another set of loci. Instead, they are to be carried out upon a single set of loci which is fixed throughout performance of all method steps.

In sum, adopting Promega's proposed construction would disengage the method steps from each other and, in doing so, conflict with the claim language, specifications, and prosecution histories. Such a result is best avoided. Phillips, 415 F.3d at 1318.

**e. Inartful Claim Drafting Does Not Require the Court to Redraft the Claims During Claim Construction**

Promega suggests that a construction limiting the loci in step (c) to the loci found in step (b) could potentially—but not of necessity—result in the "anomaly" of a dependent claim being infringed without infringement of the corresponding independent claim. Promega Br. at 19. This is because the HUMFESFPS locus is found in dependent claims 3, 4, and 5 of the '660 patent but not independent claim 1. The Court has previously commented on the possibility that this was a drafting error, and indeed it seems likely the case. *See* Sun Decl., Ex. 17 at 7. The HUMFESFPS locus originally appeared in independent claim 1 of the '660 patent, however, in

order to overcome the prior art Promega amended the claim by deleting the locus. Sun Decl., Ex. 2 at 221. It neglected, however, to make the corresponding amendment to the dependent claims.[5]

In any event, dependent claims "are only an aid to interpretation and are not conclusive." North Am. Vaccine v. Am. Cyanamid Co., 7 F.3d 1571, 1577 (Fed. Cir. 1993). Alleged anomalies in the dependent claims do not become claim construction shortcuts justifying departure from a construction rooted in the bulk of the intrinsic evidence. In other words, "[t]he dependent claim tail cannot wag the independent claim dog." Id. As discussed previously, the intrinsic evidence in this case compels a closed construction of the term "a set of . . . loci" limited to the specific loci listed in the independent claims. If the result is a dependent claim which could never be infringed because the HUMFESFPS locus appears in the dependent but not independent claims, such result would be the direct consequence of Promega's own inartful claim drafting. It must accept the result rather than ask the Court to redraft the problematic claims during claim construction in order to give effect to the dependent claims. *See* Chef Am., Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1374 (Fed. Cir. 2004) ("[C]ourts may not redraft claims, whether to make them operable or to sustain their validity. [Even] a nonsensical result does not require the court to redraft the claims.") (citations omitted).

Finally, no matter what the effect of claim construction upon dependent claims 3, 4, and 5 of the '660 patent, Promega's argument is purely theoretical. The actual potential for such an

[5] While Promega maintained that the amendment nevertheless did not exclude the HUMFESFPS locus from the scope of the claims, that assertion is invalid. Sun Decl., Ex. 2 at 8-9. Because Promega elected to draft the claim using a Markush group structure, the set of loci that is the subject of the claim can only include loci from the closed Markush group recited therein. Whether four or more loci are selected for the set, all of the loci must be selected from the closed Markush group. *Accord* Sun Decl., Ex. 16 at 2. Promega's unilateral assertion that the Markush group is open-ended and may include the HUMFESFPS locus does not make it so, particularly as it contradicts the very definition of what a Markush group is. *See* Gillete Co. v. Energizer Holdings, Inc., 405 F.3d 1367, 1372 (Fed. Cir. 2005) ("A Markush group by its nature is closed."); Norian Corp. v. Stryker Corp., 363 F.3d 1321, 1334 (Fed. Cir. 2004) ("Our case law makes it clear that closed transition phrases such as 'consisting of' are understood to exclude any elements, steps, or ingredients not specified in the claim.") (citations and internal quotations omitted).

alleged anomaly in this case is zero, as none of the accused products amplify the HUMFESPFS locus. *See* Sun II Decl., Ex. 1 (loci names indicated in the left-most column; shaded cells indicating the loci amplified for each kit). Thus, the purely hypothetical anomaly does not even bear on the infringement dispute before the Court.

**ii. "co-amplifying . . . loci"**
**"multiplex amplification . . . using . . . primers"**

| Claim Term | Defendants' Proposed Construction | Promega's Proposed Construction |
|---|---|---|
| "co-amplifying . . . loci" | when primers are used, amplifying loci together using the specific primer sequences listed in the patent | none of the asserted claims that require a multiplex of a defined set of loci exclude the use of primers other than those identified in the specification |
| "multiplex amplification . . . using . . . primers" | amplifying loci together using the specific primer sequences listed in the patent | none of the asserted claims that require a multiplex of a defined set of loci exclude the use of primers other than those identified in the specification |

**a. The Intrinsic Evidence Shows that Promega's Alleged Inventions Utilize Primers—the Specific Primers Listed in the Promega Patents**

Promega argues throughout its brief that the terms "co-amplifying . . . loci" and "multiplex amplification . . . using . . . primers" are "silent regarding 'primers.'" Promega Br. at 23; *see also* id. at 25 ("There is no mention of primers."); id. ("[T]he specification . . . makes no mention of a universal primer limitation."); id. at 27 ("The independent method claims of all four (4) Promega Patents only use the term "multiplex amplification" and say nothing about primers at all, let alone specific primers."). Promega's vigorous denial that co-amplification implicates primers is self-contradictory and wrong.

As discussed in Defendants' opening brief, Promega admitted during prosecution that "co-amplifying . . . loci" necessarily includes the use of primers. *See* Defendants Br. at 28-29. In fact, according to Promega, "the choice of oligonucleotide primers is ***critical*** to the successful operation of multiplex amplification protocols." Sun Decl., Ex. 1 at 277 (emphasis added); *see also* Defendants Br. at 22-25, Appendix C. Additionally, from the factual background section of Promega's own brief and the supporting declaration of Randall L. Dimond filed therewith, it is clear that any discussion of multiplex amplification reactions cannot escape delving substantially into primers. *See* Promega Br. at 7-9; Declaration of Randall. L. Dimond, PhD, in Support of Promega Corporation's Opening Claim Construction Brief (Dkt. #155) ("Dimond Decl."), ¶¶ 12-15. Finally, all of the examples in the specifications utilize primers to accomplish the multiplex reactions disclosed therein. *See* Sun Decl., Ex. 6 ('660 patent), cols. 20-38; Sun Decl., Ex. 7 ('598 patent), cols.11-22; Sun Decl., Ex. 8 ('235 patent), cols. 16-26; Sun Decl., Ex. 9 ('771 patent), cols. 17-26. Thus, no matter how repeatedly and emphatically Promega insists that the claims do not include primers, the evidence dictates otherwise.

Not only are primers implicated by the claims, but also the specific primer sequences listed in the Promega patents. The prosecution histories vividly depict the laborious and unpredictable state of the art and primers were certainly no exception. Promega itself declared that "the selection of primers . . . required a considerable amount of experimentation" and it was "not possible to predict which primer pairs would work well in a multiplex amplification reaction." Sun Decl., Ex. 1 at 159 (citation omitted); Sun Decl., Ex. 4 at 261 (¶ 6); *see also* Defendants Br. at 22-25, Appendix C. Consequently, it cannot be concluded that Promega actually invented all possible primers for "co-amplifying . . . loci" and for "multiplex amplification . . . using . . . primers." These claim terms must instead be construed according to

what Promega actually invented, which at most were the specific primer sequences listed in the patent for each locus. *See* Smith, 294 U.S. at 14; Acumed, 483 F.3d at 815; Phillips, 415 F.3d at 1321; Arlington Indus. V. Bridgeport Fittings, Inc., 632 F.3d 1246, 1258 (Fed. Cir. 2011) (Lourie, J., dissenting) ("The bottom line of claim construction should be that the claims should not mean more than what the specification indicates, in one way or another, the inventors invented.").

**b. The Doctrine of Claim Differentiation Does Not Trump the Intrinsic Evidence**

Promega argues on the basis of claim differentiation that the independent claims of the Promega patents cannot be construed to include specific primer sequences, because specific primer sequences are recited in the dependent claims. Promega Br. at 23. However, the doctrine of claim differentiation "is just one of many tools used by courts in the analysis of claim terms" and by itself "not a conclusive basis for construing claims." ERBE Elektromedizin GmbH v. Canady Tech., LLC, 629 F.3d 1278, 1286 (Fed. Cir. 2010); Bradford Co. v. Contevor N. Am., Inc., 603 F.3d 1262, 1271 (Fed. Cir. 2010). It "***will***," for example, "be overcome by a contrary construction dictated by the written description or prosecution history." Regents of the Univ. of Cal. v. DakoCytomation Cal., Inc., 517 F.3d 1364, 1375 (Fed. Cir. 2008) (finding that the prosecution history trumped claim differentiation as a basis for claim construction) (emphasis added) (citation and internal quotations omitted). Therefore, while Promega may rely on claim differentiation to support its proposed construction, such a shortcut can neither substitute for nor take precedence over the construction compelled by the intrinsic evidence.

As discussed above, Promega did not discover how to multiplex sets of loci using any and all possible primer sequences. The claim terms therefore should not be given an open-ended construction, even if it were to actually result in the independent claims being coextensive with

the dependent claims. Realsource, 282 Fed. Appx. at 827 ("If a patent's specification makes clear the scope of the claim language, claim differentiation cannot be used to broaden the claim's scope.") (citation omitted). As the Federal Circuit explained in Nystrom v. Trex Co., 424 F.3d 1136, 1143 (Fed. Cir. 2005):

> [S]imply noting the difference in the use of claim language does not end the matter. ***Different terms*** or phrases in separate claims ***may be construed to cover the same subject matter*** where the written description and prosecution history indicate that such a reading of the terms or phrases is proper.

*See also* Tandon Corp. v. U.S. Int'l Trade Comm'n, 831 F.3d 1017, 1136 (Fed. Cir. 1987) ("[T]wo claims which read differently can cover the same subject matter."); Edwards Lifesciences LLC v. Cook Inc., 582 F.3d 1322, 1332 (Fed. Cir. 2009) ("[C]laim differentiation is a rule of thumb that does not trump the clear import of the specification."). Any patentee can draft broad independent claims, but in order to be entitled to the full breadth of the claim she must have actually invented the claimed subject matter in the first place. The doctrine of claim differentiation cannot justify granting the patentee more than what she actually invented, as disclosed in the specification and prosecution history. It does not function as a detour around the intrinsic record to reach a proper claim construction. That is exactly the route Promega is asking the Court to take. Promega's arguments must fail and yield to the construction dictated by the intrinsic evidence.

**c. Defendants' Proposed Construction Does Not Create an Infringement Anomaly, Which in Any Event Could Not Trump the Intrinsic Evidence**

Promega next theorizes that construing the terms "co-amplifying . . . loci" and "multiplex amplification . . . using . . . primers" as Defendants propose would create an anomaly because one could potentially infringe dependent claim 3 of the '598 patent without infringing independent claim 1 from which it depends. Promega Br. at 24. Such technicalities are not a

basis for bypassing a proper and complete claim construction inquiry into the intrinsic evidence. In any case, the argument is simply wrong.

If the term "co-amplifying . . . loci" in independent claim 1 of the '598 patent is construed to include specific primer sequences, as Defendants propose, such a construction would obviously apply to dependent claim 3 as well. Claim 3 provides the further limitation wherein a specific primer sequence listed in the claim is used to co-amplify a specific locus.[6] Accordingly, in a multiplex reaction of three loci ("three-plex"), for example, one specific primer is required to satisfy the additional limitation of claim 3, but three specified primers are still required to infringe claim 3. The fact that only one primer sequence is explicitly recited in claim 3 does not mean that the other primer sequences incorporated from claim 1 are displaced or no longer apply, or that claim 3 is broader than claim 1. In Promega's exemplary three-plex, where only two specific primer sequences used, neither claim 1 nor claim 3 would be infringed. Defendants' proposed construction does not result in an infringement anomaly. Moreover, as Promega has not actually asserted any of the dependent claims reciting specific primer sequences in the present case, any such infringement anomaly would be purely hypothetical. *See* Sun II Decl., Ex. 4 (indicating the asserted claims).

**d. The Specifications of the Promega Patents Do Not Define the Claim Terms as Promega Alleges**

Promega alleges that the Promega patents provide "technical definitions" for the words "co-amplify" and "multiplex," obviating the need to construe the claim terms "co-amplifying . . . loci" and "multiplex amplification . . . using . . . primers." Promega Br. at 25. No such

[6] Whether the additional limitation creates any difference in scope between claim 1 and claim 3 is a separate issue, one that stems directly from Promega's own claim drafting. If there is indeed no difference between the claims, such a situation is perfectly acceptable. Tandon, 831 F.3d at 1136 ("[T]wo claims which read differently can cover the same subject matter."). It therefore need not alter or affect claim construction in any way. North Am. Vaccine v. Am. Cyanamid Co., 7 F.3d 1571, 1577 (Fed. Cir. 1993) ("The dependent claim tail cannot wag the independent claim dog.").

"technical definitions" are provided in any one of the Promega patents. Promega is merely attempting yet again to circumvent a proper claim construction inquiry, this time by resorting to carefully crafted sound bites.

For example, Promega asserts that the "accepted technical definition" of the word "multiplex" is "amplification of multiple loci simultaneously in a single reaction." Promega Br. at 25. This language is taken from the section of the specification entitled "Description of the Prior Art." Logically, the cited language is merely supplying a "Description of the Prior Art" rather than setting forth an affirmative definition applicable to the claimed inventions themselves. As a patentee must "clearly" define terms when acting as he own lexicographer, any doubt should be resolved against an ambiguous putative definition. CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed. Cir. 2002).

Similarly, Promega offers a nonsensical patchwork of isolated phrases selectively drawn from one of the examples in the '660 patent to provide a so-called "technical definition" of the term "co-amplify": ". . . DNA template . . . simultaneously at the individual loci . . . in a single reaction vessel." Promega Br. at 25. The full sentence reads: "In this example, a DNA template was amplified simultaneously at the individual loci D3S1539, D7S820, and D5S818 in a single reaction vessel." Sun Decl., Ex. 6 ('660 patent), col. 20, ll. 26-28. The quoted language is not a definition, *i.e.*, it does not purport to be defining any term, but rather is only providing a description of the subject matter of a single experiment. In particular, the context of the alleged definition—buried in a working example—renders it highly suspect that it is intended to function as a definition. *See* CCS Fitness, 288 F.3d at 1366 (explaining that for a patentee to act as his own lexicographer he must "***clearly*** set forth a definition of the disputed term") (emphasis added).

Typically, definitions are provided in a "Definitions" section in the initial pages of a patent. Indeed, all of the Promega patents include such a "Definitions" section. *See* Sun Decl., Ex. 6 ('660 patent), cols. 11-12; Sun Decl., Ex. 7 ('598 patent), cols. 5-6; Sun Decl., Ex. 8 ('235 patent), cols. 7-8; Sun Decl., Ex. 9 ('771 patent), cols. 7-8. Yet Promega fabricates its own "technical definitions" by stitching together words and phrases from everywhere in the specifications *except* the Definitions section. By its own hand Promega undermines its proposed claim constructions. The alleged "technical definitions" are in reality no such thing.

The fact that the Promega patents contain a Definitions section and that the alleged "technical definitions" of the words "co-amplify" and "multiplex" do not come from the Definitions section is telling. In addition, even the alleged "technical definitions" themselves support Defendants' proposed constructions. Further in the working example—or rather, "technical definition" of "co-amplify"—specific primer sequences are actually disclosed, including the reaction conditions necessary for these primers to successfully co-amplify their respective loci. Id., col. 20, ll. 39-46. Additional support is therefore provided for construing the terms "co-amplifying . . . loci" and "multiplex amplification . . . using . . . primers" to include specific primer sequences.

**iii. "primers for co-amplifying . . . loci"**
**"primers for each locus"**
**"primers flanking the loci"**

| **Defendants' Proposed Construction** | **Promega's Proposed Construction** |
|---|---|
| the specific primer sequences listed in the patent for each locus | none of the asserted claims that require a multiplex of a defined set of loci exclude the use of primers other than those identified in the specification |

Defendants incorporate by reference the discussion in Part II.A.ii.a herein.

Promega devotes substantial energy to denying the existence of "primers" in the claims of the Promega patents, in the end only to paradoxically catalogue the numerous instances of the word "primer" in the claims. *See* Promega Br. at 26. While Promega's argument regarding the employment of functional language is not altogether clear, it in any case is consistent with Defendants' proposed constructions for the three "primer" claim terms. The specifications confirm that construing these claim terms to incorporate the primer sequences in the Promega patents would not alter or interfere with the function of the primers. *See* Sun Decl., Ex. 6 ('660 patent), cols. 20-38; Sun Decl., Ex. 7 ('598 patent), cols.11-22; Sun Decl., Ex. 8 ('235 patent), cols. 16-26; Sun Decl., Ex. 9 ('771 patent), cols. 17-26. Specifically, the working examples show that successful multiplex reactions were carried out using these primer sequences, and thus that the primers continued to function in the manner contemplated by the claims. Id. In fact, the examples *only* discuss multiplex reactions using these primer sequences. Id. This reflects, consistently with the abundant intrinsic evidence already discussed, the limited scope of the alleged inventions and serves as the basis for construing the claims as proposed by Defendants.

**iv. "gel"**

| **Defendants' Proposed Construction** | **Promega's Proposed Construction** |
|---|---|
| a three-dimensional cross-linked network | a semirigid polymer, as agarose, starch, cellulose acetate, or polyacrylamide, cast into slabs or cylinders for the electrophoretic separation of proteins and nucleic acids |

A claim term should be construed as it would have been understood by "a person of ordinary skill in the art in question at the time of the invention, *i.e.*, as of the effective filing date of the patent application." Phillips, 415 F.3d at 1313. The Promega patents are a family of patents deriving from a parent application which was filed on September 30, 1994 (and

ultimately abandoned).[7] Based on new matter successively introduced in the form of continuation-in-part applications, the Promega patents are subject to earliest effective filing dates of 1994 or 1996. Therefore, the proper inquiry is how a skilled artisan in the field of multiplex amplification technology, circa 1994-1996, would have understood the term "gel."

Promega asks the Court to adopt a claim construction taken from an internet website. The website, www.dictionary.com, did not exist in the mid 1990s. *See* Sun II Decl., Ex. 2. Further, the website provides a definition of "gel" which purports to come from a Random House Dictionary bearing a copyright date of 2011. *See* Sun II Decl., Ex. 5 (not supplied by Promega in its opening brief). This reference post-dates the relevant time period by about sixteen years. It is therefore impossible that a skilled artisan's understanding of the word "gel" could actually have been based on the contemporaneous evidence now proffered by Promega. Moreover, the evidence originates from a date too far in time from the period in question to be a reliable inference point regarding the understanding of skilled artisans during the relevant time. Thus, regardless of the merits (if any) of the proffered definition, it cannot serve as the basis for claim construction of the Promega patents. Why Promega would select such an unsuitable definition is very clearly for what it does *not* include, *i.e.*, any mention of cross-linking.

Furthermore, neither www.dictionary.com nor the Random House Dictionary is a technical reference, significant because the word "gel" is also used in colloquial parlance but that fact does not make colloquial definitions appropriate in the scientific context. Indeed, the concept of a "gel" in the scientific context is far more complex. *See generally* Sun Decl., Ex. 12 (discussing gelation point, vitrification, elasticity, viscosity, various types of crosslinking, etc.); Phillips, 415 F.3d at 1321 (cautioning that reliance on dictionaries "risks transforming the

[7] U.S. Application No. 08/316,544 ("the '544 parent application"). The cover pages of the Promega patents indicate the lineage tracing back to the '544 parent application.

meaning of the claim term to the artisan into the meaning of the term in the abstract, or out of its particular context, which is the specification"). In fact, not even Promega's Vice President and Chief Technical Officer, Randall Dimond, availed himself of the internet website cited by Promega. Dr. Dimond purports to be a person skilled in the art, having provided a technology primer in his declaration in support of Promega's opening brief. *See generally* Dimond Decl. Yet in his declaration he neither relied upon nor endorsed the www.dictionary.com definition of the word "gel." He instead provided his own separate explanation. Id., ¶¶ 18-24.

In contrast to Promega's proffered construction, Defendants' proposed construction finds support in actual, published texts—the Dictionary of Polymers; Molecular Biology and Biotechnology; and Gel Electrophoresis of Proteins—rather than a single internet website. *See* Sun Decl., Exs. 12, 13, 14. The texts are, in addition, scientific references in the field of the alleged inventions rather than general purpose references, *i.e.*, they are the types of references skilled artisans would actually consult in the course of their technical labors.

The term "capillary gel electrophoresis" in a single claim (claim 6) of a single patent (the '235 patent) is a genuine anomaly. The specification of the '235 consistently distinguishes between capillary electrophoresis and gels, nowhere else mentioning "capillary gel electrophoresis." For example:

> This allows simultaneous electrophoretic analysis of several systems on the same ***gel or capillary*** electrophoresis . . . . Design of these systems is limited, in part, by the difficulty in separating multiple loci in a single ***gel or capillary***. Sun Decl., Ex. 8 ('235 patent), col. 3, ll. 27-34 (emphasis added).
>
> [A]lleles are separated, preferably, by ***gel or capillary*** electrophoresis. Id., col. 14, ll. 15-16 (emphasis added).
>
> Separation of DNA fragments in a denaturing ***polyacrylamide gel and in capillary electrophoresis*** occurs based primarily on fragment size. Once the amplified alleles are separated, the alleles and any other DNA in the ***gel or capillary*** (e.g., DNA size markers

> or an allelic ladder) can then be visualized and analyzed. Id., col. 14, ll. 62-64 (emphasis added).
>
> The products of the multiplex reactions of the present invention can be evaluated using an internal lane standard, a specialized type of size marker configured to run in the same lane of a ***polyacrylamide gel or*** same ***capillary***. Id., col. 15, ll. 34-37.

In short, capillary electrophoresis and gel electrophoresis are two distinct separation techniques. As such, whether cross-linked or uncross-linked compositions may be used in capillary electrophoresis does not bear on the issue of whether a "gel" is cross-linked. The construction of the term "gel" should not take into account non-gel-based techniques.

## B. ISSUE PRECLUSION DOES NOT APPLY TO THE SECOND CLAIM CONSTRUCTION

Promega contends that the Second Claim Construction[8] from the prior litigation (No. 01-C-244-C) between Promega and Applera Corporation (predecessor to Applied Biosystems) is binding in the instant action. To apply issue preclusion to the Second Claim Construction, Promega acknowledges that four elements must be satisfied: "(1) the issue is identical to the issue decided in the prior litigation; (2) the issue was actually litigated in the prior litigation; (3) the party against whom preclusion is sought had a full and fair opportunity to litigate the issue in the prior litigation; and ***(4) the determination of the issue was essential to a final judgment of the prior litigation***." Promega Br. at 16 (emphasis added) (citing Adair v. Sherman, 230 F.3d 890, 893 (7th Cir. 2000)).

The fourth element—"essential to a final judgment"—is not met here. Promega does not even attempt to establish it. Promega Br. at 20-21. Instead, Promega simply tries to write it out of existence. *Compare* Promega Br. at 16 ("(4) . . . essential to a final judgment") *with* Promega

[8] As used herein, the term "Second Claim Construction" refers to the Court's claim construction order dated June 7, 2002, attached as exhibit 17 to the Sun Declaration filed concurrently with Defendants' opening brief. The term "First Claim Construction" refers to the Court's claim construction dated January 2, 2002, attached as Exhibit 16 to the Sun Declaration filed concurrently with Defendants' opening brief.

Br. at 20 ("iv) substantive decision"). Promega thus does not meet the standard for claim preclusion which it concedes applies. Even if there were a final judgment from the prior litigation, Promega would still fall short of meeting its burden because it has made no attempt to show that the Second Claim Construction would be essential to it, nor is there any basis for such a showing.

Instead, Promega suggests, relying on an out-of-circuit district court decision, that issue preclusion can still apply when parties voluntarily settle because, even lacking a final judgment, finality can still be imputed to determinations made in the prior litigation. Promega Br. at 20-21. Even assuming that such decisions are relevant here, the weight of authority is to the contrary. With respect to Markman orders specifically, the court in Kollmorgen Corp. v. Yaskawa Electric Corp., 147 F. Supp. 2d 464, 468 (W.D. Va. 2001), explained that claim construction orders should not be deemed final for purposes of issue preclusion:

> As more than forty percent of all Markman orders are reversed by the Federal Circuit, logic dictates that for these claim constructions to have a preclusive effect, the litigants must first have an opportunity to seek Federal Circuit review. . . . Surely no judicial scholar would argue the Supreme Court's interests in uniformity is mutually exclusive to an interest in a proper patent claim construction.

Therefore, notwithstanding the fact that the parties had settled the earlier case, the court held that the lack of appellate review barred the application of collateral estoppel in the latter litigation. *Accord* Texas Instruments, Inc. v. Linear Techs. Corp. et al., 182 F. Supp. 2d 580, 588 (E.D. Tex. 2002) (noting that "the Kollmorgen Court makes a strong point regarding the impermanence of claim construction as a legal determination"). In Graco Children's Products, Inc. v. Regalo International, 77 F. Supp. 2d 660, 662 (E.D. Pa. 1999), the court, specifically considering the very TM Patents decision on which Promega relies, likewise held that a prior claim construction was not binding because there had been no appellate review due to the parties'

settlement. It noted interestingly that "granting preclusory effect to claim construction would encourage more appeals and discourage settlement" because even victorious plaintiffs would seek appeal in order to "correct [for purposes of future litigation] what they perceive as an unduly narrow claim construction." Id. at 664. Therefore, the fact of the parties' settlement in the Promega-Applera litigation does not impute finality to the Second Claim Construction for purposes of issue preclusion.[9]

Finally, Promega's logic that construing the claims in the instant case would permit an additional bite at the apple actually undercuts the position that the Second Claim Construction is binding. In the prior litigation, Applera Corporation and Promega had already fully litigated claim construction issues and received a First Claim Construction from the Court when Promega, dissatisfied with the outcome, sought reconsideration. This spawned a duplicative second round of briefing on the same exact issues on which the parties were already fully heard. Promega, who asked the Court to disregard the First Claim Construction in reaching the Second Claim Construction, would now restrict the Court on the basis of the Second Claim Construction from issuing a third. Yet Promega itself does not even adhere to the Second Claim Construction, but instead revises it in its proposed constructions. If additional bites at the apple are not to be permitted, then the Second Claim Construction resulting from Promega's second bite at the apple should not control in the present case. In any event, Promega cannot now object to construing the claims anew, having itself sought reconsideration in the earlier litigation.

[9] Nor does the doctrine of *stare decisis* compel the court to adhere to the Second Claim Construction. *See generally* Amgen, Inc. v. F. Hoffman-LaRoche Ltd., 494 F. Supp. 2d 54, 60 (D. Mass. 2007) ("[A] court is [only] bound to follow a higher court's applicable holding.") (citation omitted); Rambus, 569 F. Supp. 2d at 966-67 (suggesting that "it is better to get a claim construction right than it is to get a claim construction settled" and that "claim construction appears to be an exception" to the doctrine of *stare decisis*"); Sears Petrolium & Transp. Corp. v. Archer Daniels Midland Co., No. 5:03-CV-1120 (DEP), 2007 U.S. Dist. LEXIS 53576 (N.D.N.Y. July 24, 2007) (construing claim terms from the same patents in suit in a prior litigation before the same court) (attached as Exhibit 3 to the Sun II Decl. filed concurrently herewith).

## III. CONCLUSION

In light of the foregoing, Defendants respectfully request the Court to adopt their proposed claim constructions.

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## Appendix A

## Asserted Claims Which Contain[10] the Claim Term Limitations at Issue

| | Claim Term | '598 | '660 | '235 | '771 |
|---|---|---|---|---|---|
| 1 | a set of . . . loci | 1, 2, 4, 5, 7-10, 12, 15, 19, 21-24, 27, 28, 31-33 (all asserted claims) | 2-5, 9, 16, 17, 19-25, 27-31 (all asserted claims) | 1, 4, 6-13, 15-19, 21-23 (all asserted claims) | 5 (all asserted claims) |
| 2 | co-amplifying . . . loci | 1, 2, 4, 5, 7-9, 12, 15, 19, 21, 22, 28, 31, 32 | 2-5, 9, 16, 17, 19-25, 27-31 (all asserted claims) | 1, 4, 6-13, 15-18 | 5 (all asserted claims) |
| 3 | multiplex amplification . . . using . . . primers | 8 | 17 | 7-10 | none |
| 4 | primers for co-amplifying . . . loci | 8 | 25, 27-31 | 18, 19, 21-23 | 5 (all asserted claims) |
| 5 | primers for each locus | 10, 19, 23, 24, 27, 32, 33 | none | none | none |
| 6 | primers flanking the loci | none | none | 7-10 | none |
| 7 | gel | 5, 7, 22, 31, 32 | 21-23 | 6 | none |

[10] *See* 35 U.S.C. § 112, ¶ 4 ("A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.").